Gout is an inflammatory disease caused by the deposition of monosodium urate (MSU) crystals. Recently, the American College of Rheumatology (ACR) has recommended the usage of interleukin (IL)-1 inhibitor in gout patients who are refractory to typical anti-inflammatory drugs. An example of IL-1 inhibitor is canakinumab. Not much is known regarding the usage of canakinumab in gout arthritis. Thus, we decided to conduct a narrative review that summarizes the efficacy and safety of canakinumab in gout patients. In this review, we found that canakinumab is superior to non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids in treating acute gout flares. In addition, canakinumab may also be considered as a preventive therapy for gout flares in patients receiving urate-lowering therapy. Overall, canakinumab has mild side effects but may occasionally cause serious infections. Canakinumab is also generally safe for use during pregnancy. Due to the lack of studies, the safety of canakinumab in lactating women, geriatric patients, and patients with hepatic or renal impairment is still unknown.
specific populations, in this narrative review.

**Indication, dosage, and route of administration**

Canakinumab is a monoclonal antibody that inhibits IL-1β. Other than gout, canakinumab has also been indicated for Still’s disease, systemic juvenile idiopathic arthritis (sJIA), rheumatoid arthritis (RA), Muckle-Wells syndrome (MWS), and familial cold autoinflammatory syndrome (FCAS)⁹,¹⁰.

Canakinumab is a colourless to slightly brownish-yellow solution that comes in the form of a single-dose 150 mg/mL vial (to date) and is administered subcutaneously¹¹. The recommended dosage for canakinumab in treating gout flares is 150 mg, while a smaller dosage of 50 mg is enough to prevent gout attacks¹². After administration, canakinumab has a bioavailability of approximately 70% and has a half-life of 3-4 weeks¹³.

**Mechanism of action**

For gout to develop, these three steps must occur: reduced solubility, nucleation, and crystal growth. In all these steps, hyperuricemia is a necessary condition for MSU crystal deposition. Hyperuricemia could be brought about by overproduction of urate, underexcretion of urate, or a combination of both. MSU crystal deposition preferentially occurs at the first metatarsophalangeal joint, midfoot, and Achilles tendon¹.

Once MSU crystals develop, these crystals will then interact with macrophages and stimulate the release of proinflammatory IL-1β via activation of NOD-, LRR- and pyrin domain-containing protein 3 (NLPR3). Canakinumab targets IL-1β released during gout attacks and prevents its interaction with IL-1 receptors. This results in the blockage of IL-1 signalling, thus inhibiting the release of inflammatory markers, such as serum amyloid A (SAA) and C-reactive protein (CRP), as well as inhibiting neutrophil recruitment¹,¹⁴.

**Efficacy of canakinumab in gout patients**

A meta-analysis of four randomized controlled trials (RCTs) found that canakinumab significantly reduced VAS score (mean VAS score reduction = 14.59 mm; 95% CI - 19.42 to - 9.77; P < 0.001) and improved patient global assessment (PGA) scores (RR 1.478; 95% CI 1.29-1.67; P < 0.001) compared to triamcinolone acetate. Administration of canakinumab also resulted in significantly lower levels of inflammatory markers SAA (mean SAA decrease = 67.18 mg/L; 95% CI 17.06-117.31; P = 0.008) and high-sensitivity CRP (hsCRP) [mean hsCRP decrease = 15.36 mg/L; 95% CI 1.62-29.11; P = 0.03] in gout patients compared to triamcinolone acetate¹⁵.

Another meta-analysis also reported that canakinumab produced the greatest pain reduction after 2 days of treatment (mean difference to acetic acid NSAIDs = -41.12; 95% CI -53.36 to -29.11) and during the longest follow-up when compared to acetic acid derivative nonsteroidal anti-inflammatory drugs (NSAIDs) [mean difference to acetic acid NSAIDs = -12.84; 95% CI -20.76 to -4.91]. In addition, this meta-analysis also found that canakinumab is superior to intravenous and intramuscular corticosteroid in gout flare episodes¹⁶.

One RCT involving 391 patients investigated the efficacy of canakinumab in preventing gout flares during urate-lowering therapy using allopurinol. This study revealed that canakinumab (283 patients) was able to reduce the mean number of gout flares per patient by 62-72% more compared to those receiving colchicine daily (108 patients). The percentage of patients that had at least one episode of gout flare in the canakinumab group was also significantly lower compared to the colchicine group (15-27% vs. 44%; P < 0.05). Moreover, compared to colchicine, usage of 50 mg of canakinumab for 16 weeks was able to reduce the risk of flare by 64-72% (hazard ratio (HR) 0.28-0.36; P = 0.05)¹².

**Adverse events of canakinumab**

A systematic review of 654 participants that investigated the safety of canakinumab reported that there were more adverse events (AEs) in the canakinumab group compared to the triamcinolone
acetate group (57% vs. 51%; RR 1.2; 95% CI 1.1-1.4). There were also higher reports of serious AEs (SAEs) in the canakinumab group compared to the triamcinolone acetate group (6% vs. 3%; RR 2.3; 95% CI 1.0-5.2).¹⁷

Some of the common AEs reported were headache, back pain, arthralgia, hypertension, and increase in gamma-glutamyl transferase. The SAEs reported with the usage of canakinumab were mainly serious infections, such as abscesses of the jaws and limbs, pneumonia, as well as gastroenteritis.¹⁷ Currently, the longest follow-up for canakinumab use in gout patients is 24 weeks. Thus, the long-term effects of canakinumab in gout patients are still unknown.¹²,¹⁸

**Canakinumab in pregnancy and lactation**

In a systematic review of nine pregnancies exposed to canakinumab, only one experienced miscarriage (11.1% at six weeks of pregnancy).³⁹ Another review of 11 pregnancies reported that 90.9% (10 out of 11) were able to deliver at term with a mean gestational age of 38.8 weeks (37.0-40.0). Meanwhile, data for the other remaining pregnancy was unavailable. Overall, 90.0% of these pregnancies had no adverse outcome. The exceptions are two women: one developed gestational diabetes, while data was missing for the other. In addition, the babies born to these women were all healthy. There is currently no available data on the effects of canakinumab in lactating women.²⁰

**Canakinumab in geriatric patients**

One study found that the efficacy of canakinumab in reducing the rate of gout attacks between those aged ≥ 60 years (0.49 vs. 0.96; HR 0.52; 95% CI 0.37-0.72) and < 60 years (0.24 vs. 0.61; HR 0.4; 95% CI 0.24-0.66) were comparable when compared to placebo²¹. There is currently no study that specifically investigates the safety of canakinumab in geriatric patients.

**Canakinumab in patients with renal and hepatic impairment**

There are currently no formal studies investigating the use of canakinumab in patients with renal or hepatic impairment.

**2. Conclusion**

Canakinumab may be considered in patients with acute gout flares, especially in cases where NSAIDs and corticosteroids are ineffective. Moreover, canakinumab may also be considered as preventive therapy for gout flares in patients receiving urate-lowering treatment. Canakinumab is generally safe in gout patients but may occasionally cause serious infections. Thus, screening for infections, such as latent tuberculosis and viral infections, should be conducted before treatment. Overall, canakinumab is considered safe for use in pregnant women. There is currently no available data on the safety of canakinumab in lactating women, geriatric patients, and patients with hepatic or renal impairments.

**3. References**


